Multiple screening with the technicon autoanalyzer, and mass urinalysis

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SCREENING was defined as 'the presumptive identification of unrecognized disease or defect by the application of tests, examinations or other procedures, which can be applied rapidly' (Wilson and Jungner 1968).

Multiple screening may be defined as 'the application of two or more tests applied in combination to large groups of people'. The use of multiple screening tests, biochemical and haematological, to foreshadow serious disease is still being studied, but already it is evident that it has practical application in general practice today. Last (1963) suggested that a considerable amount of unsuspected disease, some of which is serious and some of which controllable, might be found fairly early in general practice, without greatly adding to the burden of the day's work. Various authors, Ashworth (1963), Scott and Robertson (1968), Davis (1968), have indicated that, as a clinician, the general practitioner is becoming more actively involved in presymptomatic diagnosis. Fry (1966) states that 'a hitherto neglected dimension of disease has been that of the large numbers of people with undiagnosed diseases'. An ever increasing number of general practitioners are entering purpose built group premises or health centres and will have adequate space and ancillary help to contemplate undertaking screening programmes.

In the United Kingdom the concept of multiple screening is not yet fully accepted by many physicians, because there is still lack of understanding of the natural history of many of the disease processes being studied. Reports have been appearing in recent years of multiple screening in the context of general practice (Cope and Smith 1967, Evans *et al* 1969, Scott and Robertson 1968, Carmalt *et al* 1970).

The present research project was planned to assess the diagnostic value of multiple tests, using the Technicon Autoanalyzer to process blood specimens from an unselected sample of 1,000 surgery attenders, aged 20 and over, between 14 March and 12 July 1968, at Finaghy Health Centre, Co. Antrim.

Description of practice and method of study

Finaghy Health Centre is situated in the southern suburbs of Belfast and serves two partnerships, each with three doctors. It was the first building in Northern Ireland specifically designed as a health centre, and was opened in 1965. With access to the Technicon Autoanalyzers at the laboratories of the Royal Victoria Hospital, it offered a well-organized base from which to launch multiple screening in a general practice population. All the patients came from one practice, which is urban, with a large social class III element.

An unselected sample of surgery attenders was obtained by a receptionist, who marked every third clinical record of patients on the appointment list of a doctor for a particular session. Such patients were asked at the time of consultation if they would be willing to participate in the investigation and there were no refusals. The doctor

recorded on a specially designed survey form, information about symptoms, provisional diagnosis, known accessory conditions, drug therapy and indicated any specific diagnostic tests which he would normally use to help in his investigation of the patient's problem. After clinical examination his nurse recorded further details: name, age, sex, date of birth, reference number, the time and date of examination, and the time in hours since the patient last had food. She then took by venepuncture 20 ml of blood from each patient. This was disposed of as follows:

1. 10 ml in a glass tube containing lithium heparin went to the biochemistry laboratory at the Royal Victoria Hospital, Belfast.
2. 4 ml in a glass tube containing potassium sequestrene went to the haematology laboratory at the same hospital.
3. 4 ml in a glass tube was dispatched to the biochemistry laboratory at the Belfast City Hospital for cholesterol estimation (males only).

Specimens were collected by hospital transport twice daily at about 1.30 p.m. and 6.30 p.m.

The serum was analysed for sodium, potassium, chloride, carbon dioxide combining power, albumin, calcium, alkaline phosphatase, bilirubin, urea, glucose, serum transaminase and cholesterol.

Haematological estimations were: haemoglobin, red cell count, packed cell volume, mean cell volume, mean corpuscular haemoglobin concentration and white cell count.

The practice nurse retained 2 ml of blood for ESR estimation at the Centre (Westergren method).

In addition to blood screening, mass urinalysis for albumin, sugar, acetone and blood was performed, using Albustix, Clinistix and Acetest reagent strips, and Occult reagent tablets, respectively.

After return of screening results and investigation, a final diagnosis was established and recorded for each case. A questionnaire was completed indicating whether or not a result (1) confirmed suspected abnormality, (2) confirmed suspected normality, (3) showed a 'wrong diagnosis', (4) showed a 'new diagnosis', (5) showed an 'unexplained abnormality'.

The clinical details recorded were coded numerically according to the 'Classification of Morbidity' prepared by the Research and Records Advisory Service of the Royal College of General Practitioners, based on the *International Classification of Diseases* (WHO, Geneva 1967). The data was transferred on to 80 column punch cards and tabulated. The answers to the questionnaire were transferred, also, on to punch cards. Patients were divided into two groups at the time of consultation:

1. Unsuspected abnormality group—tests were not specifically requested.
2. Suspected abnormality groups—tests would normally have been asked for.

An attempt was made to repeat all abnormal tests (other than those that were 'marginally abnormal') within a reasonable period of time, usually a few weeks or months, whether or not a definite diagnosis had been made.

The Technicon Autoanalyzer is the name of a laboratory machine which automatically analyses 12 blood samples by flow line processing. It became commercially available in 1957 and has revolutionized laboratory work since, by enormously increasing the work efficiency of the laboratory.

The criteria by which the diagnostic value of each screening test was assessed, were as follows:

1. Whether the test was normally requested often
2. The number of 'new diagnoses' made
3. The clinical significance of the morbidity revealed
4. The number of unexplained abnormalities recorded
5. The time spent on clinical and administrative follow-up, investigation and re-assessment.

Results

Clinical abnormalities revealed by screening tests in patients unsuspected clinically of morbidity.

1. *Blood cholesterol estimation.* To define hypercholesterolaemia is not a simple matter. Cholesterol is continuously distributed and is age related (Allerhand *et al* 1967, Bassis and Collen 1966). Age specific distributions of blood cholesterol levels among 365 males are shown in table I. The distributions are all skewed and selection of a cut-off point had to be arbitrary. Because of the daily need to assess screening results and reassure patients, it was decided before screening began to select the level of 250 mg/100 ml or greater as indicating abnormality. This was based on the work of Stamler *et al* (1966). This resulted in 105 out of 365 blood cholesterol estimations being classified as abnormal, when applied to the authors' data. Of these, 32 patients had levels greater than 290 mg/100 ml, and 20 had levels greater than 300 mg/100 ml, six of these when followed up still had levels greater than 300 mg/100 ml.

TABLE I

AGE SPECIFIC DISTRIBUTIONS OF BLOOD CHOLESTEROL LEVELS AMONG 365 MALES

	Males			
	Age in years			
	20–39		*40–59*	*60+*
	Observed	*Expected**	*Observed*	*Observed*
<125	—	—	—	—
125—	5	7.89	—	—
150—	12	19.65	1	2
175—	25	32.45	15	10
200—	46	35.66	41	20
225—	27	26.04	32	22
250—	16	12.66	26	5
275—	7	4.09	18	7
300—	3	0.87	9	8
325—	1	0.14	3	2
350+	—	—	1	1
Total	142		146	77
$X^2=16.5$ d.f.=4 $P<0.005$				

*Expected frequencies if the observations followed a normal curve.

The distributions for the two older groups are clearly skewed; that for the youngest group, 20-39, when tested, is also skewed (see table I).

In retrospect in this study one would decide to select the cut-off point for abnormality at the 95 percentile and regard the top 5 percentile as abnormal (for each age group). On this basis, to diagnose 'hypercholesterolaemia', the cut-off points would be 287 mg/100 ml, 310 mg/100 ml and 310 mg/100 ml for the age groups, 20 to 39, 40 to 59 and 60+ respectively. A new patient with a blood cholesterol estimation higher than the cut-off point of his respective age group could be regarded as abnormal. Of the 20 patients with blood cholesterol levels <300 mg/100 ml, nine were grossly obese, two were confirmed diabetics, four were suffering from mild to moderate hypertension and two of slight build had previously had myocardial infarcts.

2. Table II shows the distribution and assessment of abnormal blood biochemical screening tests in patients unsuspected clinically of disease. The tests in this table were considered to be of little diagnostic value in the present study. They were sodium, potassium, chloride, total protein, albumin and serum transaminase (SGOT). Apart from SGOT estimation (which was requested twice), they were never requested for diagnostic purposes, and no 'new diagnosis' emerged. Over 90 per cent of the results of all these biochemical tests were normal, yet there were still considerable numbers of suggested abnormalities, most of these were not associated with detectable disease. Some may have been due to imprecise definition of the 'normal ranges', others may have resulted from technical error. Table II shows that there were eight patients with unexplained raised serum transaminase values (5 female, 3 male), seven of which were normal when repeated a month later. One new diagnosis of drug toxic hepatitis resulted from the use of this test. A female, aged 54, who had been undergoing treatment for acid-fast cervical adenitis with Pasinah tablets (tabs ii qid) and Isoniazid (100 mg tid), was found to have an SGOT value of 140 IU/litre, which when repeated two weeks later was 134 IU/litre. Following cessation of treatment, a month later, it was 8 IU/litre.

Abnormal results, unassociated with evident clinical abnormalities, which subsequently were found to be normal, were assumed to be due to technical error. Out of 956 SGOT estimations, eight fell into this category, so the test was considered to be technically accurate.

3. Table III shows the assessment of other abnormal blood biochemical results by sex in the unsuspected abnormality group. All the tests shown, except blood glucose, were considered to be of doubtful diagnostic value in the present study. These were blood calcium, alkaline phosphatase, bilirubin, carbon dioxide combining power and blood urea.

Calcium. This test was requested once for diagnostic purposes in a 33-year-old male with a history of renal colic. When used simply as a screening test, no new diagnosis resulted. Out of 388 male estimations nine (2.3 per cent) were abnormal and unexplained. Out of 599 female estimations 24 (4.3 per cent) were the same (*see* table III). Yet of these 33 results, only one follow-up result in a female, aged 62, remained abnormal and unexplained. Although this test did not prove to be of any diagnostic value, it perhaps should be included in general practice or community screening to pick up the rare case of hypercalcaemia due to hyperparathyroidism (once in 6–8,000 patients, Collen 1968, p. 57).

Alkaline phosphatase. It was requested three times as a diagnostic test. Used as a screening test, it did not produce a 'new diagnosis'. Out of 401 male estimations ten (2.5 per cent) were abnormal and unexplained. Out of 578 female estimations 13 (2.2 per cent) were the same (table III). Eight out of ten unexplained abnormal alkaline phosphatase results were repeated, and of these four remained abnormal and unexplained. Out of 13 female abnormal unexplained results, eight were repeated, and of these three remained abnormal and unexplained. There were two abnormal results, 1 male and 1 female, which were explicable by the clinical condition of the patients.

Bilirubin. This test was normally requested only once in 982 screening estimations and confirmed a clinical impression of jaundice in a female age 67, who turned out to have obstructive jaundice. Out of 401 male estimations 49 (12.2 per cent) were unexplained and abnormal. Out of 580 female estimations 15 (2.6 per cent) were the same (*see* table III). Overall, 58 of these 64 abnormal results were repeated (i.e. in both sexes), and of these, 43 were normal, 14 were only 'marginally abnormal', and only one remained grossly abnormal due to lipaemic serum. Of the 14 patients with marginally abnormal results, none showed clinical evidence of disease of liver or biliary

TABLE II

NORMAL RANGES OF VALUES, DISTRIBUTION OF NORMAL AND ABNORMAL BLOOD BIOCHEMICAL RESULTS BY SEX, IN THE UNSUSPECTED ABNORMALITY GROUP

Blood test	*Sex*	*Normal range of values*	*Normal*		*Abnormal*					*Grand total*
			Total	*Per-centage*	*New diagnoses*	*Explained*	*Unexplained*	*Abnormal Total*	*Per-centage*	
Sodium	M	136–145 mEq/1	374	*98.4*	0	0	6	6	*1.6*	380
	F		530	*96.5*	0	0	19	19	*3.5*	520
Potassium	M	3.6–5.0 mEq/1	357	*94.2*	0	0	22	22	*5.8*	379
	F		537	*96.2*	0	0	21	21	*3.8*	558
Chloride	M	95–108 mEq/1	354	*95.4*	0	0	17	17	*4.6*	371
	F		492	*92.8*	0	0	38	38	*7.2*	530
Total protein	M	6.3–8.0 gm/100 ml	363	*90.6*	0	1	37	38	*9.4*	401
	F		436	*92.1*	0	2	44	46	*7.9*	582
Albumin	M	3.3–5.2 gm/100 ml	392	*97.8*	0	1	8	9	*2.2*	401
	F		560	*96.4*	0	1	20	21	*3.6*	581
SGOT	M	5–45 IU/1	389	*99.2*	0	0	3	3	*0.8*	392
	F		558	*98.9*	1	0	5	6	*1.1*	564

TABLE III

NORMAL RANGES OF VALUES, DISTRIBUTION OF NORMAL AND ABNORMAL BLOOD BIOCHEMICAL RESULTS BY SEX, IN THE UNSUSPECTED ABNORMALITY GROUP

Blood test	*Sex*	*Normal range of values*	*Normal*		*Abnormal*					*Grand total*
			Total	*Per-centage*	*New diagnoses*	*Explained*	*Unexplained*	*Abnormal Total*	*Abnormal Per-centage*	
Calcium	M	8.8–10.5 mg/100 ml	379	*97.7*	0	0	9	9	*2.3*	388
	F		535	*95.7*	0	0	24	24	*4.3*	559
Alkaline phosphatase	M	4–16 K.A. units/ 100 ml	390	*97.3*	0	1	10	11	*2.7*	401
	F		564	*97.6*	0	1	13	14	*2.4*	578
Bilirubin	M	0.0–1.0 mg/100 ml	350	*87.3*	2	0	49	51	*12.7*	401
	F		563	*97.1*	2	0	15	17	*2.7*	580
Carbon dioxide combining power	M	24–32 mEq/1	370	*99.2*	0	0	3	3	*0.8*	373
	F		509	*94.1*	0	0	32	32	*5.9*	541
Urea	M	19–45 mg/100 ml	357	*89.7*	0	0	41	41	*10.3*	398
	F		557	*96.7*	1	2	18	21	*3.6*	578
Glucose..	M	<110 mg/100 ml fasting (=4 hours after food or longer) <180 mg per cent after a meal	351	*95.7*	5	4	7	16	*4.3*	367
	F		533	*98.0*	3	4	4	11	*2.0*	544

tract. Four 'new diagnoses' emerged—cases of Gilbert's syndrome—(constitutional unconjugated hyperbilirubinaemia) which were diagnosed after consideration on the following criteria.

1. The presence of unconjugated hyperbilirubinaemia
2. A history of recurrent malaise, characterized by periods of nausea and occasionally vomiting
3. A mild icteric tinge in the conjunctiva of the eyes
4. Normal liver function tests, normal plasma protein electrophoresis, normal reticulocyte count and no excess of urobilinogen in an afternoon specimen of urine. This condition is difficult to detect in a family from the history alone, because of the mildness of the jaundice.

Apart from these four cases of Gilbert's syndrome, the bilirubin test was disappointing as a screening test and it would appear to be subject to gross technical error.

Urea. This test was normally requested six times and was used 976 times as a screening test.

One 'new diagnosis' of subacute glomerulonephritis was made in a female aged 38, who consulted the doctor in April 1968 with complaints of tiredness and vague chest tightness, but did not complain of any urinary symptoms, had no oedema, and was not hypertensive. Her blood urea was 66 mg/100 ml and remained persistently raised for several months.

Table III shows the abnormal results, two female results were explicable by the clinical condition of each patient, but 41 male results out of 357 were unexplained, as were 18 female results out of 557. These 59 patients were re-called, examined clinically, BP estimation was done, MSU, and repeat blood urea were sent to the laboratory.

Of these, 20 out of 41 male results were still abnormal and eight out of 18 female results were also abnormal. Table IV shows the distribution of these repeat unexplained abnormal blood urea results by age and sex, and it can be seen that the proportion increases greatly over the age of 50 in each sex. Of the 20 male cases, seven had hypertension, one had diabetes, but none showed clinical signs of renal impairment, and similarly with the eight females, only one suffered from hypertension, but none showed signs of renal failure. These patients were either suffering from occult renal disease or their urea values were simply rising with age. This relationship with age has been confirmed by many workers (Kaufman *et al* 1969, Allerhand *et al* 1967). These findings illustrate the difficulty in selecting blood urea screening levels for abnormality, especially over the age of 50, and the problems of investigation of abnormal results for occult renal disease.

TABLE IV
DISTRIBUTION OF REPEAT UNEXPLAINED ABNORMAL BLOOD UREA RESULTS BY AGE AND SEX

Age group	*Repeat unexplained abnormal blood urea results*			
	Male		*Female*	
	No.	*Per cent*	*No.*	*Per cent*
20—	0	*0.0*	0	*0.0*
30—	0	*0.0*	1	*12.5*
40—	1	*5.0*	0	*0.0*
50—	4	*20.0*	2	*25.0*
60—	6	*30.0*	2	*25.0*
70+	9	*45.0*	3	*37.5*
Total	20	*100.0*	8	*100.0*

Carbon dioxide combining power (CO_2 CP). This test was normally requested twice to confirm respiratory failure in two men with chronic bronchitis.

Table III shows the classification of abnormal CO_2 CP results in the unsuspected abnormality group. Out of 373 male results three (0.8 per cent) were unexplained and 32 out of 541 (5.9 per cent) female results were the same. These were nearly all low levels and occurred in clinically healthy young females.

Glucose. Out of 924 glucose estimations, 911 were not normally requested and table III shows the results—eight new diabetics were discovered. These were patients

with abnormal blood sugar levels, whose glucose tolerance tests were judged abnormal by the following criteria:

Fasting level	110 mg/100 ml or greater
1 hour level	170 mg/100 ml or greater
2 hour level	120 mg/100 ml or greater

If these three criteria were fulfilled, then diabetes was diagnosed. These are similar to the criteria suggested by Remein and Wilkerson (1961).

Of the eight previously unknown diabetics five were men. Of these, three were severe diabetics with two-hour glucose tolerance test (GTT) levels 145 mg/100 ml or greater, and two were 'borderline diabetics' with two-hour GTT levels 120 mg/100 ml or greater. These patients were all obese, but did not mention the classical diabetic symptoms of thirst or polyuria.

The three new female cases of diabetes were all classed as severe, judged by the two-hour GTT levels mentioned above. There were only 11 false positive screening results, seven men and four women, out of 911 screening tests. These were patients who had no clinical evidence of diabetes, whose screening results were abnormal, but whose GTT's were normal. Eight known patients with diabetes, four men and four women, had abnormally high blood sugars.

Unlike other screening tests, e.g. blood urea, the number of false positive tests was small, and GTT's were easy to perform, compared with more complicated and time-consuming renal investigations. The yield of significant morbidity was relatively high and the present study indicated clearly that blood screening techniques were more sensitive than urinalysis to detect unsuspected diabetes. Five diabetics, three men and two women, would not have been detected by urinalysis alone, as they did not have glycosuria. The blood glucose test was considered to be of definite value in the present study although as McKeown and Knox (1968) stated 'more evidence is needed of the prognostic significance of hyperglycaemia and of the effectiveness of its early treatment in the absence of signs'.

Haematology

Haemoglobin estimation. The World Health Organization (1959) recommended that anaemia should be considered to exist when the Hb value is less than 14 gm/100 ml in men and less than 12 gm/100 ml in women. Normal range of Hb values accepted for the present study, men 14–18 gm/100 ml., women 12–16 gm/100 ml.

The laboratory did 960 estimations and in 900 cases the test was not normally requested (unsuspected abnormality group). Table V shows the distribution of normal and abnormal haemoglobin results and of new diagnosis by sex in two groups.

(a) Unsuspected abnormality group;
(b) Suspected abnormality group.

In group (a) anaemia was diagnosed in 48 out of 380 males screened (12.6 per cent) and in 58 out of 520 females (11.1 per cent). Many of these results were 'marginally abnormal' and not of great clinical significance.

Out of 106 anaemias revealed by screening, 95 were investigated fully (clinical examination, occult blood in stools, rectal and vaginal examinations), before treatment was given for several months with tabs Ferro-Redoxin i tid (ferrous sulphate 136 mg, ascorbic acid 50 mg.)

In the follow-up examination of 32 men with anaemia, the Hb had risen in 25, was the same in two, had fallen in five, but 15 were still 'marginally anaemic'. The latter were symptomless and felt well. There was an increase in the mean Hb value from 12.8 gm/100 ml at the intial survey to 13.6 gm/100 ml at the follow up.

In the follow up of 63 women with anaemia, the Hb had risen in 57 and fallen in

TABLE V

DISTRIBUTION OF NORMAL AND ABNORMAL HAEMOGLOBIN RESULTS AND OF NEW DIAGNOSES BY SEX IN TWO GROUPS

(a) unsuspected abnormality group
(b) suspected abnormality group

Sex	*New diagnoses*		*Abnormal results*				*Total*		*Normal results*		*Grand total*
			Explained		*Unexplained*						
	No.	*Per cent*	*No.*	*Per cent*	*No.*	*Per cent*	*No.*	*Per cent*	*No.*	*Per cent*	
	(a) unsuspected abnormality group (tests not requested)										
M	48	*12.6*	2	*0.5*	3	*0.7*	53	*13.8*	327	*86.2*	380
F	58	*11.1*	1	*0.2*	0	*0.0*	59	*11.3*	461	*88.7*	520
Total	106	*11.8*	3	*0.3*	3	*0.3*	112	*12.4*	788	*87.6*	900
	(b) suspected abnormality group (tests requested)										
M	2	*25.0*	3	*37.5*	0	*0.0*	5	*62.5*	3	*37.5*	8
F	3	*5.8*	19	*36.5*	0	*0.0*	22	*42.3*	30	*57.7*	52
Total	5	*8.3*	22	*36.7*	0	*0.0*	27	*45.0*	33	*55.0*	60

six, but 12 were still anaemic. There was an increase in the mean Hb value from 11.1 gm/100 ml initially to 13.0 gm/100 ml subsequently.

All these cases were iron-deficiency anaemia—52.3 per cent of the males and 59.4 per cent of the females were idiopathic in aetiology, 12 cases (18.8 per cent) in females were due to menorrhagia, and anaemia of pregnancy accounted for 17.1 per cent of cases. No new case of cancer was discovered as the result of detecting anaemia, but three men known to be suffering from malignant lesions were found to be anaemic.

Table V (b) shows the results when anaemia was suspected clinically. It is interesting to note that only five diagnoses were confirmed and 33 times the test failed to give an abnormal result. Other components of the full blood count were studied in detail, but are not reported here, as the Hb estimation was taken as the main index of anaemia. These were, the red cell count, packed cell volume, mean cell volume and mean corpuscular haemoglobin concentration.

Blood sedimentation rate—Westergren method. The normal range accepted for this study was, for males 0–15 mm/hour and for females 0–20 mm/hour.

Table VI summarizes the normal and abnormal results of this test in two groups (a) unsuspected; (b) suspected abnormality group. The latter shows that the test was requested 42 times and no new diagnosis was established. There were two unexplained high ESR's in two female patients.

On 16 occasions, seven men and nine women, a raised ESR confirmed a condition already diagnosed clinically and was of value in assessing the inflammatory activity of the condition (*see* table VI (b)).

In (a) unsuspected abnormality group, table VI shows that abnormal explained results were obtained in 117 patients, 41 male (13.4 per cent) and 76 female (16.8 per cent). These were associated with insignificant and self-limiting indispositions, and none of the conditions diagnosed had any serious clinical significance, yet such patients had to be followed up and observed for return to 'normal' health.

Fourteen men and nine women had unexplained high ESR's for several weeks, but subsequent follow-up showed that only two were abnormal and unexplained a few

TABLE VI

DISTRIBUTION OF NORMAL AND ABNORMAL BLOOD SEDIMENTATION RESULTS, AND OF NEW DIAGNOSES BY SEX IN TWO GROUPS

(a) unsuspected abnormality group
(b) suspected abnormality group

Sex	*New diagnoses*		*Abnormal results*				*Total*		*Normal results*		*Grand total*
			Explained		*Unexplained*						
	No.	*Per cent*	*No.*	*Per cent*	*No.*	*Per cent*	*No.*	*Per cent*	*No.*	*Per cent*	
	(a) unsuspected abnormality group (tests not requested)										
M	5	*1.6*	41	*13.4*	14	*4.7*	60	*19.7*	245	*80.3*	305
F	4	*0.9*	76	*16.8*	9	*2.0*	89	*19.7*	363	*80.3*	452
Total	9	*1.2*	117	*15.5*	23	*3.0*	149	*19.7*	608	*80.3*	757
	(b) suspected abnormality group (tests requested)										
M	0	*0.0*	7	*70.0*	0	*0.0*	7	*70.0*	3	*30.0*	10
F	0	*0.0*	9	*28.1*	2	*6.3*	11	*34.4*	21	*65.6*	32
Total	0	*0.0*	16	*38.1*	2	*4.8*	18	*42.9*	24	*57.1*	42

months later. These normal follow-up results also indicated, as above, that the ESR was of doubtful diagnostic value in the present investigation, because no condition of clinical significance was detected.

Urinalysis results

Table VII shows a summary of the results of mass urinalysis performed with the blood screening programme.

TABLE VII

SUMMARY OF RESULTS OF URINALYSIS

Results	*No. of patients*		
	Males	*Females*	*Total*
	399	575	974
Glycosuria—Known diabetics	2	3	5
—Others	15	7	22
Albuminuria	11	31	42
Ketonuria	0	0	0
Haematuria	2	1	3
Total	30	42	72

A urine contained significant amounts of albumin, if it reacted positively to Albustix reagent strip and showed turbidity, when boiled.

Albuminuria. Of 950 patients screened (both sexes), 42 (4.3 per cent) had albuminuria. Of these nine women and two men had acute urinary infection, only one woman was discovered with chronic urinary infection, and three women and two men had albuminuria associated with known chronic urinary disease. Twelve women and five men had transient albuminuria, unassociated with confirmed infection or clinical abnormality. Of the remainder two women with albuminuria were not investigated and six patients, four women and two men, had albuminuria associated with disease of other organs of the body.

Glycosuria. A urine contained significant amount of sugar if it reacted positively to Clinistix reagent strip.

Of 974 patients screened (both sexes) 22 (2.2 per cent) had glycosuria (excluding five known diabetics with glycosuria). Of these, three men and one woman were new diabetics (0.4 per cent), and three men and one woman had renal glycosuria (normal GTTs). Glycosuria of pregnancy occurred twice (normal GTTs). It was found that

11 patients, eight men and three women had transient glycosuria unassociated with any clinical abnormality, and one man with glycosuria was not investigated.

Haematuria. A urine contained significant amount of blood if it reacted positively to Occultest reagent tablets.

Nine hundred and sixty-four screening tests were performed.

Males: Two cases of acute pyelitis. Both had albuminuria.

Females: All tests were normal.

Kentonuria. A urine contained significant amounts of acetone if it reacted positively to Acetest reagent strip.

Nine hundred and sixty-nine screening tests were performed, and all were normal.

Discussion

The present investigation showed how successfully multiple biochemical and haematological screening (Technicon Autoanalyzer), could be performed in a general practice. Smaller surveys, carried out satisfactorily, have been reported recently by other workers (Scott and Robertson 1968, Carmalt *et al*, 1970). This study was organized by an active general practitioner, who, assisted ably by his practice nurses, performed multiple screening procedures. It emphasized the need for:

1. the provision of adequate accommodation and ancillary help
2. adequate time to assess cases, administer the screening programme and follow up suggested abnormalities.

As Scott and Robertson (1968) indicated, a qualified nurse should be able to cope with the range of screening procedures used in multiple screening in general practice. The author confirmed this finding, and found the nurse invaluable also in follow-up work, and communication of normal results to patients.

The present project worked smoothly, collection of specimens became a daily routine, and prompt communication of results was achieved without difficulty. A few bottles were broken in transit or lost, and a small percentage of blood specimens were reported as 'lipaemic' or 'haemolysed'.

The most significant finding in the present study was the disappointing yield of 'new diagnoses' of clinical significance, i.e. requiring adjustment of the patients' management and therapy, in the unsuspected abnormality group; eight unsuspected diabetics, all over 40, 20 patients with hypercholesterolaemia (>300 mg/100 ml), 11 with iron deficiency anaemia (<11 g/100 ml), one woman with chronic urinary infection and one with subacute glomerulonephritis. This represents a total of 41 cases out of 1,000 screened (4.1 per cent). By contrast, Carmalt *et al* (1970), found that unrequested tests led to a 'new diagnosis' of clinical significance in 16.9 per cent of patients. Scott and Robertson (1968) reported a 'substantial amount of morbidity' in a multiple screening survey in an Edinburgh general practice.

Another significant finding in the present investigation was the large number of marginally positive screening results, which often remained unexplained. Many were assumed to be due to imprecise definition of the 'normal' ranges and some to technical error. These facts led the author to classify the following blood tests used in the present study as of little diagnostic value. They should probably not be included in the range of tests offered for general practice screening: sodium, potassium, chloride, total plasma protein, plasma albumin and serum transaminase (SGOT). Mass urinalysis for ketonuria and haematuria was also of little diagnostic value and could not be recommended for inclusion. The poor yield of significant unsuspected morbidity in this study was partly due to the inclusion in the 12 channel Technicon Autoanalyzer of tests, e.g. electrolytes, much more commonly requested in hospital work than in general practice. The same facts, to a lesser degree, suggested the following blood tests were of doubtful diagnostic

value in the present survey; calcium, alkaline phosphates, bilirubin, carbon dioxide combining power, and urea. In this group significant findings were the high percentage of false positive blood urea results, the absence of unknown cases of severe uraemia, the higher prevalence of positive blood urea screening results in men than women, which rose with increasing age. This was confirmed by Kaufman *et al* (1969). Because of these findings, the author would not recommend the inclusion of the blood urea test in a range of screening tests for use in general practice.

The author feels that the calcium estimation should be included to pick up the rare condition of hypercalcaemia due to parathyroid tumour (one in 6—8,000 patients, Collen, 1968, p. 57).

Another significant finding was that serum bilirubin screening was disappointing (apart from four unsuspected Gilbert's syndromes) and subject to gross technical error. Lipaemic and haemolysed sera were reported not infrequently and caused false positive results.

Present findings with the CO_2 CP estimation indicated that the 'normal' range 24–32 mEq/litre was inaccurate and that the lower limit of 'normal' for females should be much lower.

Unlike Rardin's finding (1966) the alkaline phosphatase estimation in the present work was technically very precise and it was significant that it brought under observation seven patients with persistently raised values which were still unexplained after intensive hospital investigations.

The author, on the evidence of the present survey, would not include the ESR estimation in a range of tests for general practice. It was valuable for assessing activity of disease, but not for diagnosis. By contrast, Pincherle and Shanks (1967) thought it was a valuable screening test, after a screening survey of 1,739 'normal' men in the Institute of Directors' Medical Centre, London. In the present study, however, the test revealed large numbers of abnormal results in patients who were suffering from apparently trivial illnesses, most of which were self-limiting and not serious.

The prevalence of mild degrees of anaemia in women of child bearing age in the unsuspected abnormality group (*see* Table V (a)), confirmed the lack of close correlation between symptoms, physical signs and haemoglobin levels (Wood and Elwood 1966) and that such levels of anaemia might only be detected by blood screening techniques. A single estimation might indicate anaemia, but it was advisable to follow up patients and to repeat estimations. Then, a falling Hb value, or failure of the anaemia to respond adequately to treatment, would call for deeper investigation. Other workers (Kilpatrick and Hardisty 1961) have shown a marked rise in haemoglobin levels in a group of patients after treatment of anaemia with oral iron for several months. The present work confirmed this, and suggested that, despite Wood and Elwood's findings, it was worth while still to correct iron deficiency. Treatment was successful, appreciated, easy to perform and economical. The author would classify the haemoglobin estimation as a test of definite clinical value for use in general practice.

This study emphasized the superiority, in detecting new diabetics, of blood glucose screening, compared with testing for glycosuria on its own. The Royal College of General Practitioners' Diabetic Survey (1962) showed that mass urinalysis for glycosuria did not uncover the potential or latent diabetic with intermittent or slight glycosuria. The present work indicated that five out of eight unsuspected diabetics found, would not have been detected by urinalysis alone, as they did not have glycosuria. These results when analysed, corroborated the view of McKeown and Knox (1968) and 'more evidence is needed of the prognostic significance of hyperglycaemia, and of the effectiveness of its early treatment in the absence of signs'. The blood glucose estimation was considered to be a most useful diagnostic test and should be included in a range of

multiple tests for use in general practice. All the diabetics discovered by the present survey were over 40 and tending to obesity. This suggests the need for some selection of at-risk patients before screening, by directing screening efforts at middle-aged-elderly patients.

The high prevalence of hypercholesterolaemia in the present survey suggested the need for more base-line data about middle-aged patients liable to coronary artery disease. It was not easy to define the condition (*see* Results above) but, in retrospect in this study, cut-off points for serum cholesterol abnormality for different male age-groups have been suggested (women were not studied for cholesterol values). The recommended levels are higher than the level of 250 mg/ml used by American epidemiologists and based on the work of Stamler *et al* (1966). Various workers (Kannel *et al* 1961, Schafer 1964, Stamler *et al* 1966) have shown the correlation between coronary artery disease and hypercholesterolaemia, and Warner and Shumway (1968) have demonstrated how common high cholesterol blood values are in the community. This was shown, also, by the present investigation. The author recommends, that as a test of definite value, the blood cholesterol estimation should be included as a screening procedure in everyday clinical practice in the community.

Mass urinalysis performed as part of the present research project revealed a sizeable number of patients with glycosuria and albuminuria, as did a similar survey by Baddeley *et al* (1964). In each survey, a small percentage of new diabetics was found by detecting unsuspected glycosuria (0.4 per cent, present study, compared with 0.2 per cent, Baddeley *et al* 1964).

Screening for ketonuria and haematuria was unrewarding in both these surveys, and the author would not recommend such testing. Haematuria was invariably associated with albuminuria, and the test for the latter was all that was required. The author found that a high proportion of cases had transient albuminuria due to acute infection, and women were much more affected than men. This was less obvious in the study by Baddeley *et al* (1964). One woman, unsuspected of carrying chronic urinary infection, was discovered in this study. The above results indicated, that mass urinalysis, using Albustix and Clinistix reagent strips to detect albuminuria and glycosuria respectively, was worthwhile. It was cheap, easy to perform, and a few cases of significant morbidity were revealed.

Accumulation of scientific data in the present study had greatly stimulated the doctors concerned to further examine clinically many patients and has added greatly to the background knowledge of each patient. Base line data have been recorded from which change in the future can be observed. Experience gained confirmed that screening tests are seldom diagnostic, but merely arouse suspicion of disease. Much time was needed for recording and communicating results. Hodes (1969) regards the computer as a 'fundamental tool' in this respect if large scale screening is to be put on a practical basis. As described earlier, multiple screening of large groups in general practice is now feasible, and would be much easier to perform with computer help, but further research is needed to establish its value to the community. Meanwhile more and more general practitioners are making daily use of diagnostic laboratory facilities. Wade and Elmes (1969) have shown that 85 per cent of their diagnostic procedures at their medical outpatients, Belfast City Hospital, were unnecessary, because these could have been performed at the modern group clinic or health centre. They described briefly a small pilot scheme at Finaghy Health Centre that was started in 1966. The diagnostic facilities of the centre were supplemented by full radiological and laboratory facilities at the above hospital. The results of this scheme persuaded them to undertake an analysis of the work of their outpatient clinic, with the result reported above. If general practitioners could relieve hospital outpatient clinics on a large scale, by coping with over 80 per cent of less complex investigations at present being performed there, they

would render an excellent service to the community and would enhance their own clinical status at the same time.

The present trend in general practice towards larger partnerships and groups working in health centres, accounts to some extent for the enhanced interest of many general practitioners in laboratory and other diagnostic facilities. In discussing this development note must be taken of the attitudes of undergraduates who will not be attracted to a career in general practice unless such facilities are freely available. Furthermore, they have been introduced to concepts of comprehensive care and group responsibility and an increasing number will wish to exercise more fully 'preventive' skills, as well as the traditional 'curative' skills.

In conclusion, this study of multiple laboratory screening, proved its feasibility in general practice, but the author would recommend in present circumstances further research into selective screening of specific age and sex groups. This should be aimed at early diagnosis of a limited number of diseases or pathological conditions: anaemia, diabetes, renal disease and hypercholesterolaemia.

Summary

To assess the diagnostic value of multiple biochemical and haematological screening procedures in general practice, an investigation was carried out on an unselected sample of 1,000 surgery attenders, aged 20 and over, at Finaghy Health Centre, Co. Antrim. This included a mass urinalysis survey. The value of each screening test was assessed by the clinical significance of unsuspected morbidity, the number of new diagnoses, and the number of unexplained abnormalities found. Patients were classified into two groups:

1. Unsuspected abnormality group—diagnostic tests were not requested.
2. Suspected abnormality group—specific investigation had been asked for.

The yield of significant and unsuspected morbidity in group (1) was studied and discussed, as were the practical difficulties encountered in the survey.

As a result of this investigation the tests performed were divided into three categories:

1. Those of little diagnostic value: blood estimations of sodium, potassium, chloride, total plasma protein, plasma albumin and serum transaminase; also, urinalysis for ketonuria and haematuria.

2. Those of doubtful diagnostic value: blood estimation of calcium, alkaline phosphatase, bilirubin, carbon dioxide combining power, blood urea and blood sedimentation rate.

3. Those of definite value: blood sugar, haemoglobin and blood cholesterol values; also, mass urinalysis for albuminuria and glycosuria.

This study suggested that in present circumstances in general practice further research into selective multiple laboratory screening of specific age and sex groups should be considered and directed at presymptomatic diagnosis of a limited number of diseases or pathological states: anaemia, diabetes, renal diseases and hypercholesterolaemia.

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OF DOG DAYS

For Physick is either curative or preventive; Preventive we call that which by purging noxious humors, and the causes of diseases, preventeth sickness in the healthy, or the recourse thereof in the valetudinary; this is of common use at the spring and fall, and we commend not the same at this season. Therapeutick or curative Physick, we term that, which restoreth the Patient unto Sanity, and taketh away diseases actually affecting. Now of diseases some are cronical and of long duration, as quartane Agues, Scurvy, etc. Wherein because they admit of delay we defer the cure to more advantagious seasons: Others we term acute, that is, of short duration and danger, as Fevers, Pleurisies, etc. In which, because delay is dangerous, and they arise unto their state before the Dog-daies determine, we apply present remedies according unto Indications; respecting rather the acuteness of the disease, and precipitancy of occasion, then the rising or setting of Stars; the effects of the one being disputable, of the other assured and inevitable.

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